## REMARKS

I. Status of the Claims

Upon entry of the amendment claims 119 and 127 are pending. Claim 119 is amended herewith. Support for the amendment is to claim 119 is replete in the specification including, e.g., page 43, lines 8-9 and page 116, line 19 to page 117, line 24. Claim 127 is withdrawn from consideration as directed to a non-elected invention. The amendment or cancellation of claims is made without prejudice to future prosecution.

II. Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 121-126 were rejected as allegedly introducing new matter. Applicants disagree, and respectfully submit these claims are fully supported in the specification as filed. However, to expedite prosecution Applicants have cancelled these claims. The cancellation is without prejudice to prosecuting claims directed to this subject matter in this or a related application.

Claims 119-126 were rejected as allegedly not enabled by the specification. This rejection is moot as it applies to claims 120-126. Applicants respectfully traverse this rejection as it applies to claim 119.

The bases for the rejection of these claims are, as Applicants understand them from pages 6-12 of the Office Action:

- Allegedly one of skill could not obtain a representative number of polynucleotides falling within the claim without undue experimentation. This is in part because "the claims are drawn broadly to a very large genus of polynucleotides . . .".
- Allegedly the specification provides insufficient guidance to enable the skilled artisan to determine which alterations in any TRT can be made without altering the functional properties of the encoded protein, in part because even a single conservative amino acid substitution can adversely affect biological activity.

Applicants will address each of these bases in turn.

***No undue experimentation is required to make the claimed polynucleotides***

The instant claims are directed to polynucleotides encoding a protein defined by structure (a degree of identity to a reference protein and the presence of six amino acid motifs identified by the inventors) and function (an assayable activity). Applicants respectfully submit the specification provides both the prototype sequence and activity assays, and clearly enables one of ordinary skill to make active variants without undue experimentation. It appears Applicants and the Office are in agreement that the specification enables assays for telomerase activity and methods of mutagenesis of nucleic acids (see Office Action mailed April 9, 2004, at page 9). Further, it is not disputed the specification provides the reference sequence (SEQ ID NO:118) and teaches the TRT motifs recited in claim 119. Applicants submit one with knowledge of the instant specification could, using only routine molecular biology techniques, introduce mutations into SEQ ID NO:118 while retaining the TRT motifs or otherwise identify a nucleic acid encoding a protein at least 60% identical to SEQ ID NO:118 and containing the TRT motifs. One of ordinary skill with knowledge of the instant specification would be able to identify those encoded proteins having telomerase activity. Numerous mutation strategies were know to scientists at the time the claimed invention was made. The standard texts *Protocols in Molecular Biology* (Ausubel et al. eds.) and *Molecular Cloning: A Laboratory Manual* (Sambrook et al. eds.) describe techniques employing chemical mutagenesis, cassette mutagenesis, degenerate oligonucleotides, mutually priming oligonucleotides, linker-scanning mutagenesis, alanine-scanning mutagenesis, and error-prone PCR. Other efficient methods include the *E. coli* mutator strains of Stratagene (Greener et al., Methods Mol. Biol. 57:375, 1996) and the DNA shuffling technique described by W.P.C. Stemmer (*Proc. Natl. Acad. Sci. USA* 91:10747, 1994; and *Nature* 370:389, 1994; also see Patten et al., *Curr. Opin. Biotechnol.* 8:724, 1997). Using the DNA shuffling technique, the encoding regions are fragmented, annealed under low stringency conditions, and then amplified by PCR. These methods can be used to create variants, the amplified DNA would next be introduced into a an expression cassette (described in the specification at, *e.g.*, pages 168-200), and then transfected into *E. coli,* thereby producing a library of thousands of variant TRT cDNAs. In view of the known variability of naturally occurring TRT sequences, a substantial proportion of the artificial variants would be expected to

retain telomerase activity. Applicants submit it would not be unduly burdensome to construct a library of thousands of TRT variants based on the reference sequence, using any one of several techniques known in the art at the time this application was filed. The library could then be easily screened using assays described in the specification to identify variants with telomerase activity.

The Office has recognized that a claimed genus of polynucleotides can be properly defined by reference to a prototype sequence and an activity of an encoded protein, and the Office commonly grants claims in which a claimed polynucleotide is defined by structure and function. For example, in a recent decision, the Board of Patent Appeals and Interferences found that a claim for a polynucleotide having at least 80% sequence identity to a prototype sequence (An isolated . . . wee1 polynucleotide having at least 80% sequence identity to the entire coding region of SEQ ID NO:1 . . .) was both described and enabled. *Ex parte Yuejin Sun et al.* (BPAI 2003, Appeal No. 2003-1993; copy enclosed). Although this opinion was not written for publication and is not binding precedent of the Board, Applicants submit the reasoning articulated in the opinion is nonetheless useful in addressing the merits of the present case. In *Ex parte Sun*, the examiner had argued the claim was not enabled because "the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" and the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in alteration of the plant's phenotype." The Board reversed the rejection, observing that the specification provided the chemical *structure* of a polynucleotide that comprises the coding sequence set forth in SEQ ID NO:1, provided an example of *how to screen* for WEE1 activity, and observed that "most of the variations in the amino acid sequence of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. *In the present case, the specification provides the "chemical structure" of the reference sequence, describes assay methods, and* not only *provides guidance as to which regions from the TRT protein are*

*conserved, but* requires *in the claim that the motifs be present in the claimed variants.* Applicants submit the presently claimed invention is enabled by the guidance found in the specification.

Further, Applicants believe the Office has not established that it would require undue experimentation to make and use the variants using the methods suggested by the Applicants. Rather, the Office takes the position, as Applicants understand it, that the genus encompassed by the claims is so large that "screening all natural and non-natural variants of TRT . . . is not considered routine." First, this seems to focus on the *number* of variants to be screened. As the CAFC has noted, a considerable amount of screening (*e.g.*, screening numerous hybridomas for monoclonal antibodies) is not necessarily *undue* experimentation. Second, Applicants submit that screening all variants is not the proper measure of enablement. Many issued claims to chemical compounds, for example, call out structures in which various constituents are defined by R groups. These claims can encompass a large number of compounds. Given the nature of organic synthesis it could take considerable effort (if even possible) to make all members of the genus. This does not render such claims not enabled. Similarly, as noted above, numerous issued and presumptively enabled patents include claims to polynucleotides defined by percent identity to a reference sequence and a biological activity. In some cases it might take considerable effort to make each and every polynucleotides in the genus but, again, this does not render such claims not enabled.

***The specification provides sufficient guidance for making variants***

The Office also asserted that the specification provides insufficient guidance for making variants, in part because even a single conservative amino acid substitution can adversely affect biological activity. It is no doubt true that in some proteins even a single conservative amino acid substitution at a catalytic site can adversely affect biological activity. It is equally true, however, that in many proteins *most* substitutions do not eliminate activity and many substitutions can increase activity. In the case of the subject matter of this application, telomerase reverse transcriptase, the instant specification provides striking evidence that a ***considerable amount of variation*** is tolerated in catalytically active telomerase proteins. The

specification describes the sequences of six telomerase proteins, with highly diverse sequences. Mouse TRT, for example, has only about 64% identity to human TRT and TRT sequences in different eukaryotes can have identities of less than 30%, and yet perform essentially the same function. One of skill in the art would ascertain from this teaching that a wide range of substitutions, deletions, etc. would be tolerated while retaining activity, provided the characteristic motifs are present.

Further, the specification provides ample guidance to one of ordinary skill in the art, e.g., a molecular biologist or protein chemist, for making variants. The application provides an extensive comparison of sequences: One skilled in the art would recognize that alterations to non-conserved regions would less likely adversely affect activity as compared to alterations in conserved regions. The specification teaches in detail that telomerases share common features in the form of structural motifs, which motifs are described in detail. The specification also describes examples of a variety of conservative substitutions that could be made that would have a higher likelihood of not disrupting the activity of the encoded protein (see, e.g., page 113, line to page 114, line 19). The Office has referred to only a single example of a variant not having telomerase catalytic activity, the 182-bp deletion variant *lacking* the motifs required by the claim and *identified* in the specification not having telomerase catalytic activity.

Applicants have provided several examples of TRT proteins with diverse sequences, demonstrating a considerable amount of variation is tolerated in catalytically active telomerase proteins. Applicants have described the motifs that characterize catalytically active telomerase proteins and has claimed polynucleotides with reference to both function and structure, *including the presence of the mofits* which are recited in the pending claim. The skilled artisan using routine molecular biological techniques and assays taught in the specification could make and use the claimed polynucleotides. The enablement requirement of Section 112 does not require more. For these reasons, Applicants respectfully submit this rejection should be withdrawn.

III. Claim Rejections under 35 USC 112, Second Paragraph

Claims 121-126 were rejected as allegedly indefinite. This rejection is now moot in view of the cancellation without prejudice of these claims.

IV. Claim Rejections under 35 USC 102(e)

Claims 119-126 were rejected as anticipated under 35 USC 102(e) by U.S. Pat. No. 6,093,809 and U.S. Pat. No. 6,309,867 (each having the same specification). These patents disclose the TRT proteins of Euplotes aediculatus, Schizaromyces, Saccharomyces and human. Of these, the Euplotes, Schizaromyces, and Saccharomyces proteins cannot anticipate claim 119, because none is at least 60% identical to SEQ. ID NO:118 when the entire sequence of said protein is optimally aligned with SEQ ID NO:118. The maximal amino acid identity for the most closely matched subsequences is approximately 21%, 21% and 25%, respectively, between SEQ ID NO:118 and *Euplotes aedicaulatus*, *Schizosccharomyces pombe*, and *Saccharomyces cerevisiae* proteins.[1]

SEQ ID NO:118 is the human TRT sequence. The human TRT sequence is disclosed and claimed in US Pat. No. 6,309,867, having the same inventorship as the instant application. Accordingly Applicants submit the disclosure of human TRT in U.S. Pat. No. 6,093,809 and U.S. Pat. No. 6,309,867 is not "by another" as required by 102(e).

**V. Claim Rejections under 35 USC 102(a)**

Claim 119 was rejected under 35 USC 102(a) in view of either Lingner (describing p123 of *Euplotes*) or Lendvay (describing EST2 of *S. cerevisiae*). However, neither reference described nucleic acids encoding a polypeptide with at least 60% sequence identity to SEQ ID NO:118. For this reason, neither reference anticipated the present invention.

**VI. Claim Rejections under Obviousness Type Double Patenting**

Claims 119-126 were rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 3, 4 and 7-10 of U.S. Patent No. 6,261,836. Applicants will file

[1]BLAST alignments of the sequences are provided in the Appendix to this response. Alignments of only portions of the TRT sequences are aligned (the level of sequence identity in other regions apparently is too low for any meaningful alignment and inclusion of these regions would result in a *lower* percentage of identity). In the case of the *Schizosccharomyces pombe* sequence, two different regions are aligned (having sequence identities of 23% and 25%.)

a terminal disclaimer or take other appropriate action upon indication that the application is otherwise in condition for allowance.

Claims 119-126 were rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 3, 4 and 7-10 of U.S. Patent No. 6,093,809. The Office states the present claims are drawn to polynucleotides encompassed by the genus now claimed. The '809 patent disclosed the TRT sequences for *Euplotes aedicaulatus* and *S. cerevisiae*. As explained above Applicants have previously explained that these sequences share little identify with SEQ ID NO:118 and are not encompassed by the instant claims. Accordingly, it is requested that this rejection be withdrawn.

Claims 119-126 were rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,767,719, which describes mouse TRT. The Office correctly asserts that the polynucleotides of the '719 patent are encompassed by claim 119. The Office argues that the polynucleotides claimed in the '719 patent anticipate the instantly claimed polynucleotides (as a species anticipates a genus) and thus render the instant claims obvious.

Using the one-way test for obviousness to determine whether a double-patenting rejection is appropriate, the question is whether the polynucleotides of the '719 patent (encoding mouse TRT) are an *obvious variant* of the polynucleotides claimed in the instant application. Applicants submit the "mouse" TRT polynucleotides of the '719 patent are not an obvious variant of the claimed polynucleotides. That is, one apprised of the pending generic claims would not find the specific mouse sequence obvious. Thus, under the one-way obviousness test, no double-patenting rejection is appropriate. In determining whether a one-way or two-way obviousness test is used, the MPEP discusses two situations in which double patenting between a patent and an application might occur, *i.e.*, when the filing date of the patent is later than the application and when the filing date of the patent is earlier than the application. *Neither* situation is present here, as the instant application and the application underlying the '719 patent both were filed on November 19, 1997. The Applicant could not have prosecuted the claims in a single application because they are separately owned. Both applications were diligently prosecuted and concurrently prosecuted. Further, issuance of a patent from the instant application will not result

in patent term beyond the expiration of the '719 patent. For these reasons, this double patenting rejection should be withdrawn.

VII. Rejoinder of Claim 127

Claim 127 is directed to a method of increasing proliferative capacity in vitro. Claim 127 is a method claim that depends and incorporates the limitations of product claim 119. Accordingly, upon establishing that claim 119 is free of prior art, then claim 127 will also be free of prior art. For this reason, applicants request that claim 127 be rejoined into the group under examination, in accordance with MPEP § 821.04.

## CONCLUSION

Applicants respectfully request that all rejections be reconsidered and withdrawn.

Respectfully submitted,

Date: June 23, 2005

Randolph T. Apple
Reg. No. 36,429

Appendix: Sequence Alignments

Enclosure: *Ex parte Sun et al.*

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 303-571-4000
Fax: 415-576-0300

60477402 v3

015389-002950US

# Blast 2 Sequences results

PubMed Entrez BLAST OMIM Taxonomy Structure

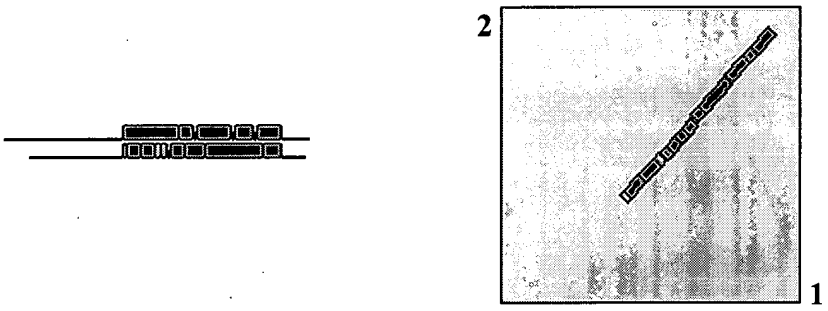
Query: Human
vs.
Subject: *Euplotes*

**BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]**

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter ☐ Align

**Sequence 1** lcl|seq_1 **Length** 1126 (1 .. 1126)

**Sequence 2** lcl|seq_2 **Length** 1031 (1 .. 1031)




NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

Score = 157 bits (398), Expect = 2e-36
Identities = 127/589 (21%), Positives = 245/589 (41%), Gaps = 41/589 (6%)

```
Query: 460  FVRACLRRLVPPGLWGSRHNERRFLRNTKKFISLGKHAKLSLQELTWKMSVRDCAWLRRS 519
            F+      ++P      R N + F +  KK++ L KH  +    L  K++ R+ +W++
Sbjct: 361  FINEFFYNILPKDFLTGR-NRKNFQKKVKKYVELNKHELIHKNLLLEKINTREISWMQVE 419

Query: 520  PGVGCVPAAEHRLREEILAKFLHWLMSVYVVELLRSFFYVTETTFQKNRLFFYRKSVWSK 579
                     +H     +L K L W+    VV L+R FFYVTE     ++ ++YRK++W
Sbjct: 420  TSAKHFYYFDHE-NIYVLWKLLRWIFEDLVVSLIRCFFYVTEQQKSYSKTYYYRKNIWDV 478

Query: 580  LQSIGIRQHLKRVQLRELSEAEVRQHREARPALLTSRLRFIPKPDGLRPIVNMDYVVGAR 639
            +  + I   LK+  L E+ E EV + +++       +LR IPK    RPI+  +     +
Sbjct: 479  IMKMSIAD-LKKETLAEVQEKEVEEWKKSL-GFAPGKLRLIPKKTTFRPIMTFN----KK 532

Query: 640  TFRREKRAERLTSRVKALFSVLNYERARR---PGLLGASVLGLDDIHRAWRTFVLRVRAQ 696
                +++  +LT+  K L S L  +  +        G +V   DD+ + + +  FV + + Q
Sbjct: 533  IVNSDRKTTKLTTNTKLLNSHLMLKTLKNRMFKDPFGFAVFNYDDVMKKYEEFVCKWK-Q 591

Query: 697  DPPPELYFVKVDVTGAYDTIPQDRLTEVI--------------ASIIKPQNTYCVRRYAV 742
               P+L+F  +D+   YD++ +++L+  +               A I+K +N   +
Sbjct: 592  VGQPKLFFATMDIEKCYDSVNREKLSTFLKTTKLLSSDFWIMTAQILKRKNNIVIDSKNF 651

Query: 743  VQKAAHGHVRKAFKSHVSTLTDLQPYMRQFVAHLQETSPLRDAVVIEQSSSLNEASSGLF 802
             +K    + R+ F+  ++      P +   + Q     +  +++E           L
Sbjct: 652  RKKEMKDYFRQKFQK-IALEGGQYPTLFSVLENEQNDLNAKKTLIVEAKQRNYFKKDNLL 710

Query: 803  DVFLRFMCHHAVRIRGKSYVQCQGIPQGSILSTLLCSLCYGDMENKLFAGIRRD------ 856
               +    ++ +   GK Y Q +GIPQG  +S++L S   Y  +E      +R +
```

```
Sbjct: 711  QPVINICQYNYIINFNGKFYKQTKGIPQGLCVSSILSSFYYATLEESSLGFLRDESMNPEN 770

Query: 857  ---GLLLRLVDDFLLVTPHLTHAKTFLRTLVRGVPEYGCVVNLRKTVVNFPVEDEALGGT 913
             LL+RL DD+LL+T    +A  F+  L+    E G   N++K   +FP+
Sbjct: 771  PNVNLLMRLTDDYLLITTQENNAVLFIEKLINVSRENGFKFNMKKLQTSFPLSPSKFAKY 830

Query: 914  AFVQMPAHGLF----PWCGLLLDTRTLEVQSDYSSYARTSIRASLTFNRGFKAGRNMRRK 969
             +    +      W G+ +D +TL +  + +      I  +L  N   K      +K
Sbjct: 831  GMDSVEEQNIVQDYCDWIGISIDMKTLALMPNINLRIE-GILCTLNLNMQTKKASMWLKK 889

Query: 970  LFGVLRLKCHSLFLDLQVNSLQTVCTNIYKILLLQAYRFHACVLQLPFH 1018
                  +   + +    + +       + K+ +   Y++  C  +   H
Sbjct: 890  KLKSFLMNNITHYFRKTITTEDFANKTLNKLFISGGYKYMQCAKEYKDH 938

CPU time:     0.06 user secs.       0.01 sys. secs          0.07 total secs.

Lambda     K      H
   0.324    0.138    0.435

Gapped
Lambda     K      H
   0.267   0.0410    0.140


Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Sequences: 1
Number of Hits to DB: 5827
Number of extensions: 4015
Number of successful extensions: 7
Number of sequences better than 10.0: 1
Number of HSP's better than 10.0 without gapping: 1
Number of HSP's gapped: 2
Number of HSP's successfully gapped: 1
Number of extra gapped extensions for HSPs above 10.0: 0
Length of query: 1126
Length of database: 871,278,970
Length adjustment: 142
Effective length of query: 984
Effective length of database: 871,278,828
Effective search space: 857338366752
Effective search space used: 857338366752
Neighboring words threshold: 9
Window for multiple hits: 0
X1: 15 ( 7.0 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 40 (21.6 bits)
S2: 83 (36.6 bits)
```

015389-002950US

# Blast 2 Sequences results

Query: Human
vs.
Subject: *Saccharomyces*

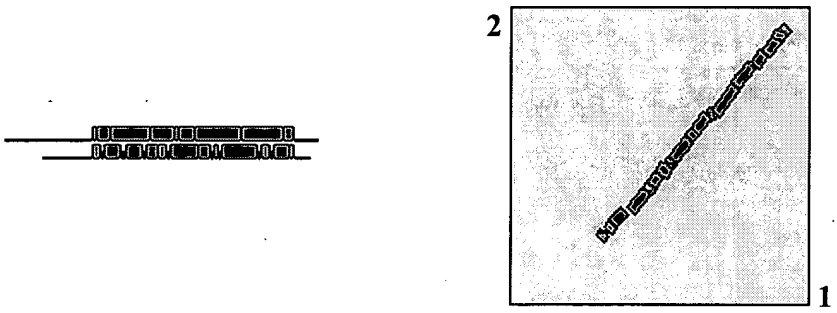
PubMed Entrez BLAST OMIM Taxonomy Structure

**BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]**

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter ☐ Align

**Sequence 1** lcl|seq_1 **Length** 1126 (1 .. 1126)

**Sequence 2** lcl|seq_2 **Length** 884 (1 .. 884)




NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

```
Score =  110 bits (274), Expect = 6e-22
Identities = 150/714 (21%), Positives = 283/714 (39%), Gaps = 101/714 (14%)

Query: 341  FLLSSLRPSLTGARRLV---ETIFLGSRPWMPGTPRRLPRLPQRYWQMRPLFLE-LLGNH 396
            F  S + PS +  ++L    E IF          P  L ++PQR      L L+ LL  H
Sbjct: 199  FPYSKILPSSSSIKKLTDLREAIF----------PTNLVKIPQRLKVRINLTLQKLLKRH 248

Query: 397  AQCPYGVLLKTHCPLRAAVTPAAGVCAREKPQGSVAAPEEEDTDPRRLVQLLRQHSSPWQ 456
             +  Y  +L + CP            +R+ P+                          +
Sbjct: 249  KRLNYVSILNSICPPLEGTVLDLSHLSRQSPKE-------------------------R 282

Query: 457  VYGFVRACLRRLVPPGLWGSRHNERRFLRNTKKFISLGKHAKLSLQELTWKMSVRDCAWL 516
            V  F+   L++L+P  ++GS+ N+ + ++N    +SL  +  L    L  K+ ++D  WL
Sbjct: 283  VLKFIIVILQKLLPQEMFGSKKNKGKIIKNLNLLLSLPLNGYLPFDSLLKKLRLKDFRWL 342

Query: 517  RRSPGVGCVPAAEHRLR--EEILAKFLHWLMSVYVVELLRSFFYVTETTFQKNRLFFYRK 574
                 +  +H      ++   F+ WL    + +++++FFY TE +     + ++R
Sbjct: 343  ----FISDIWFTKHNFENLNQLAICFISWLFRQLIPKIIQTFFYCTEIS-STVTIVYFRH 397

Query: 575  SVWSKLQSIGIRQHLKRVQLRELSEAEV-RQHREARPALLT-SRLRFIPKPDGLRPIVNM 632
              W+KL +  I ++ K      L E  V R H      +    S++R IPK        +
Sbjct: 398  DTWNKLITPFIVEYFKTY----LVENNVCRNHNSYTLSNFNHSKMRIIPKKSNNEFRIIA 453

Query: 633  DYVVGARTFRREKRAERLTSRVKALFSVLNYERARRPGLLGA--SVLGLDDIHRAWRTFV 690
                GA          E   + ++    +L Y R +RP       S   + D  + ++  +
Sbjct: 454  IPCRGADEEEFTIYKENHKNAIQPTQKILEYLRNKRPTSFTKIYSPTQIADRIKEFKQRL 513

Query: 691  LRVRAQDPPPELYFVKVDVTGAYDTIPQDRLTEVIASIIKPQNTYCVRRYAVVQKAAHGH 750
            L+ +  +  PELYF+K DV   YD+IP+     ++   +K +N + VR
```

```
Sbjct: 514  LK-KFNNVLPELYFMKFDVKSCYDSIPRMECMRILKDALKNENGFFVRS---------- 561

Query: 751  VRKAFKSHVSTLTDLQPYMRQFVAHLQETSPLRDAVVIEQSSSLNEASSGLFDVFLRFMC 810
             +  F ++   L       + F        P    + I+   +++ ++  + +V    +
Sbjct: 562  -QYFFNTNTGVL-------KLFNVVNASRVPKPYELYIDNVRTVHLSNQDVINVVEMEIF 613

Query: 811  HHAVRIRGKSYVQCQGIPQGSILSTLLCSLCYGDM---ENKLFAGIRRDGLLLRLVDDFL 867
               A+ +  K Y++  G+ QGS LS  +  L Y D+    ++  A   +D L+L+L DDFL
Sbjct: 614  KTALWVEDKCYIREDGLFQGSSLSAPIVDLVYDDLLEFYSEFKASPSQDTLILKLADDFL 673

Query: 868  LVTPHLTHAKTFLRTLVRGVPEYGCVVNLRKTVVNFPVEDEALGGTAFVQMPAHGLFPWC 927
             +++          +  + G  +Y    N  K +      D+             +  +C
Sbjct: 674  IISTDQQQVINIKKLAMGGFQKYNAKANRDKILAVSSQSDD----------DTVIQFC 721

Query: 928  GLLLDTRTLEVQSDYSSYARTSIRASLTFNRGFKAGRNMRRKLFGVLRLKCHSLFLDLQV 987
             + +  + LEV    S+     IR+        K+ + + R L  +   +     +D  +
Sbjct: 722  AMHIFVKELEVWKHSSTMNNFHIRS--------KSSKGIFRSLIALFNTRISYKTIDTNL 773

Query: 988  NSLQTVCTNIYKIL--LLQAYRFHACVLQLPFHQQVWKNPTFFLRVISDTASLC 1039
             NS  TV   I  ++  + + Y+     L +   Q + +  +F  R+I  T S C
Sbjct: 774  NSTNTVLMQIDHVVKNISECYKSAFKDLSINVTQNM-QFHSFLQRIIEMTVSGC 826
```

CPU time: 0.06 user secs. 0.01 sys. secs 0.07 total secs.

| Lambda | K | H |
|---|---|---|
| 0.324 | 0.138 | 0.435 |

Gapped

| Lambda | K | H |
|---|---|---|
| 0.267 | 0.0410 | 0.140 |

Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Sequences: 1
Number of Hits to DB: 5476
Number of extensions: 3844
Number of successful extensions: 5
Number of sequences better than 10.0: 1
Number of HSP's better than 10.0 without gapping: 1
Number of HSP's gapped: 1
Number of HSP's successfully gapped: 1
Number of extra gapped extensions for HSPs above 10.0: 0
Length of query: 1126
Length of database: 871,278,970
Length adjustment: 142
Effective length of query: 984
Effective length of database: 871,278,828
Effective search space: 857338366752
Effective search space used: 857338366752
Neighboring words threshold: 9
Window for multiple hits: 0
X1: 15 ( 7.0 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 40 (21.6 bits)
S2: 83 (36.6 bits)

015389-002950US

# Blast 2 Sequences results

Query: Human
vs.
Subject: *Schizosaccharomyces*

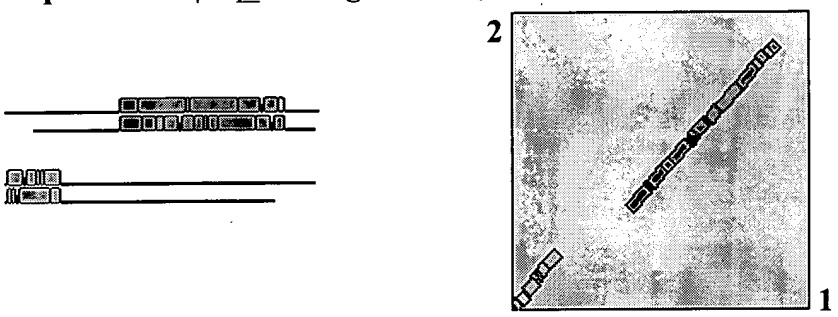


**BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]**

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter ☐ Align

**Sequence 1** lcl|seq_1 **Length** 1126 (1 .. 1126)

**Sequence 2** lcl|seq_2 **Length** 988 (1 .. 988)




NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

```
Score =  193 bits (491), Expect = 4e-47
Identities = 147/573 (25%), Positives = 276/573 (47%), Gaps = 47/573 (8%)
```

```
Query: 446  QLLRQHSSPWQVYGFVRACLRRLVPPGLWGSRHNERRFLRNTKKFISLGKHAKLSLQELT 505
            ++L     P QV+ F+R+ L R+ P  +WG++       L++ + F+ L ++   SL  L
Sbjct: 332  KILSYSLKPNQVFAFLRSILVRVFPKLIWGNQRIFEIILKDLETFLKLSRYESFSLHYLM 391

Query: 506  WKMSVRDCAWL---RRSPGVGCVPAAEHRLREEILAKFLHWLMSVYVVELLRSFFYVTET 562
              + + +  WL    +RS     C+   ++    R++I A+F++WL + +++ +L+SFFY+TE+
Sbjct: 392  SNIKISEIEWLVLGKRSNAKMCL--SDFEKRKQIFAEFIYWLYNSFIIPILQSFFYITES 449

Query: 563  TFQKNRLFFYRKSVWSKLQSIGIRQHLKRVQLRELSEAEVRQHREARPALLTSRLRFIPK 622
            +  +NR  ++RK +W KL         +K      +++E  VR   + +  L  + +R +PK
Sbjct: 450  SDLRNRTVYFRKDIW-KLLCRPFITSMKMEAFEKINENNVRMDTQ-KTTLPPAVIRLLPK 507

Query: 623  PDGLRPIVNMDYVVGARTFRREKRAERLTSRVKALFSVLNYERARRPGLLGASVLGLD-- 680
             + R I N+      +    +K         ++ + S+L +         L+     G+
Sbjct: 508  KNTFRLITNLRKRFLIKMGSNKKMLVSTNQTLRPVASILKH-------LINEESSGIPFN 560

Query: 681  -DIHRAWRTF---VLRVRAQDPPPELYFVKVDVTGAYDTIPQDRLTEVIASIIKPQNTYC 736
             +++     TF    +L+ R       + YFV++D+    YD I QD +  ++    +K    +
Sbjct: 561  LEVYMKLLTFKKDLLKHRMFG--RKKYFVRIDIKSCYDRIKQDLMFRIVKKKLKDPE-FV 617

Query: 737  VRRYAVVQKAAHGHVRKAFKSHVSTLTDLQPYMRQFVAHLQETSPLRDAVVIEQSSSLNE 796
            +R+YA +  A      K F S   +  D+ P+ +       +TS   D + ++       +
Sbjct: 618  IRKYATIH-ATSDRATKNFVSEAFSYFDMVPFEKVVQLLSMKTS---DTLFVDFVDYWTK 673

Query: 797  ASSGLFDVFLRFMCHHAVRIRGKSYVQCQGIPQGSILSTLLCSLCYGDMENKLFAGIRRD 856
            +SS +F +    +  H V+I    Y+Q  GIPQGSILS+ LC     D+ ++  +  +  ++
```

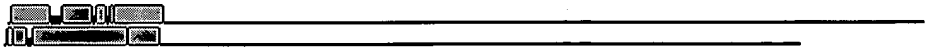
```
Sbjct: 674  SSSEIFKMLKEHLSGHIVKIGNSQYLQKVGIPQGSILSSFLCHFYMEDLIDEYLSFTKKK 733

Query: 857  G-LLLRLVDDFLLVTPHLTHAKTFLRTLVRGVPEYGCVVNLRKTVVNFPVEDEALGGTAF 915
            G +LLR+VDDFL +T +   AK FL   +RG  ++    +L KTV+NF   +  +  T F
Sbjct: 734  GSVLLRVVDDFLFITVNKKDAKKFLNLSLRGFEKHNFSTSLEKTVINFENSNGIINNTFF 793

Query: 916  VQMPAHGLFPWCGLLLDTRTLEV-----QSDYSSYARTSIRASLTFNRGFKAGRNMRRKL 970
             +       P+ G  ++ R+L+       + D + +  TS+  +    + F
Sbjct: 794  NESKKR--MPFFGFSVNMRSLDTLLACPKIDEALFNSTSVELTKHMGKSF---------F 842

Query: 971  FGVLRLKCHS---LFLDLQVNSLQTVCTNIYKI 1000
            + +LR    S   +F+D+  NS    C NIY++
Sbjct: 843  YKILRSSLASFAQVFIDITHNSKFNSCCNIYRL 875

Score = 37.0 bits (84), Expect = 6.4
Identities = 44/191 (23%), Positives = 80/191 (41%), Gaps = 30/191 (15%)
```



```
Query: 5    PRCRAVRSLLRSHYREVLPLATFVRRLGPQGWRLVQRGDPAAFRALVAQCL--------- 55
            P+ R +R  L + Y  +  L  +V+       LV RG PA+  + + + L
Sbjct: 7    PKSRILR-FLENQYVYLCTLNDYVQ--------LVLRGSPASSYSNICERLRSDVQTSFS 57

Query: 56   -----VCVPWDARPPPAAPSFRQVSCLKELVARVLQRLCERG---AKNVLAFGFALL--D 105
                  V +D++P               EL+A V++++ +      +N+L  GF++   D
Sbjct: 58   IFLHSTVVGFDSKPDEGVQFSSPKCSQSELIANVVKQMFDESFERRRNLLMKGFSMNHED 117

Query: 106  GRGPP-EAFTTSVRSYLPNTVTDALRGSGAWGLLLRRVGDDVLVHLLARCALFVLVAPSC 164
             R          + S  PN +   L     W LLL  +G D + +LL++ ++F  +
Sbjct: 118  FRAMHVNGVQNDLVSTFPNYLISILESKN-WQLLLEIIGSDAMHYLLSKGSIFEALPNDN 176

Query: 165  AYQVCGPPLYQ 175
             Q+ G PL++
Sbjct: 177  YLQISGIPLFK 187

CPU time:     0.07 user secs.       0.00 sys. secs          0.07 total secs.

Lambda     K      H
   0.324    0.138    0.435

Gapped
Lambda     K      H
   0.267   0.0410    0.140


Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Sequences: 1
Number of Hits to DB: 6168
Number of extensions: 4333
Number of successful extensions: 8
Number of sequences better than 10.0: 1
Number of HSP's better than 10.0 without gapping: 1
Number of HSP's gapped: 3
Number of HSP's successfully gapped: 2
Number of extra gapped extensions for HSPs above 10.0: 0
Length of query: 1126
Length of database: 871,278,970
Length adjustment: 142
Effective length of query: 984
```

```
Effective length of database: 871,278,828
Effective search space: 857338366752
Effective search space used: 857338366752
Neighboring words threshold: 9
Window for multiple hits: 0
X1: 15 ( 7.0 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 40 (21.6 bits)
S2: 83 (36.6 bits)
```